# Complete Summary

## GUIDELINE TITLE

American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer.

## BIBLIOGRAPHIC SOURCE(S)

Benson AB 3rd, Schrag D, Somerfield MR, Cohen AM, Figueredo AT, Flynn PJ, Krzyzanowska MK, Maroun J, McAllister P, Van Cutsem E, Brouwers M, Charette M, Haller DG. American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer. J Clin Oncol 2004 Aug 15;22(16):3408-19. [45 references] PubMed

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Stage II colon cancer

### GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness

### CLINICAL SPECIALTY

Colon and Rectal Surgery
Gastroenterology
Oncology

### INTENDED USERS

Physicians

## GUIDELINE OBJECTIVE(S)

- To address whether all medically fit patients with curatively resected stage II colon cancer should be offered adjuvant chemotherapy as part of routine clinical practice
- To identify patients with poor prognosis characteristics
- To describe strategies for oncologists to use to discuss adjuvant chemotherapy in practice

## TARGET POPULATION

Patients with curatively resected stage II colon cancer

## INTERVENTIONS AND PRACTICES CONSIDERED

### Consideration of Adjuvant Chemotherapy

1. Not recommended for routine use
2. Identification of high-risk patients who may benefit including:
    - Patients with inadequately sampled lymph nodes
    - T4 lesions
    - Perforation
    - Poorly differentiated histology
3. Patient discussion/education strategies:
    - Points of discussion include:
        - Amount of prognostic information the patient wishes to receive
        - Patient perception of risks and benefits
        - Potential incremental (relative and absolute) improvement in cure rate conveyed as numbers or as words
        - Potential risks (chemotherapy over 6 to 8 months), late toxicities, and treatment-related deaths.
        - Effect of comorbidities on potential benefit versus potential risk
        - Numeracy program (www.mayoclinic.com/calcs)
4. Encouragement of patient participation in clinical trials

## MAJOR OUTCOMES CONSIDERED

- Overall survival
- Disease-free survival
- Treatment toxicity outcomes

# METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

## DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Cancer Care Ontario (CCO) Systematic Review

The systematic review of the literature on the role of adjuvant therapy in stage II colon cancer conducted by the Cancer Care Ontario Practice Guideline Initiative (CCOPGI) Gastrointestinal Cancer Disease Site Group served as the primary source of evidence for this guideline. The original CCOPGI systematic review of this topic was published in 1997. After discussions with the American Society Clinical Oncology (ASCO), CCOPGI staff undertook an update of the evidence on the use of adjuvant therapy in stage II colon cancer. This process was completed in January 2003, and the updated systematic review was published in the Journal of Clinical Oncology. Articles were selected for inclusion in the CCO systematic review evidence if they met the following criteria: (1) randomized controlled trials (RCTs) with appropriate control groups, or (2) meta-analyses of RCTs comparing adjuvant therapy with observation in patients with stage II colon cancer who had undergone surgery with curative intent.

## NUMBER OF SOURCE DOCUMENTS

37 randomized controlled trials and 11 meta-analyses of adjuvant chemotherapy or immunotherapy for colon cancer

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

## METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The American Society of Clinical Oncology (ASCO) Panel reviewed all publications identified by the Cancer Care Ontario (CCO) review to select randomized phase III trials pertinent to its deliberations. Based on consultation from the Methodology Subcommittee of ASCO´s Health Services Committee (HSC), the Panel focused attention on randomized trials that included a surgery-alone control arm and at least one fluorouracil (FU)-based chemotherapy arm. The Panel designed a coding sheet to complete the review of the randomized trials included in the Cancer Care Ontario Practice Guideline Initiative (CCOPGI) systematic review, and the Co-Chairs assigned each Panel member a subset of articles to review. In addition, authors were contacted by the Panel to facilitate disaggregation of results for stage II and stage III patients in the original reports. Several of the studies identified are only currently available in abstract form. The CCOPGI authors, at the request of the ASCO Expert Panel, completed a literature-based (versus an

individual patient data–based) meta-analysis of trials that included a surgery-alone control arm and at least one FU-based chemotherapy arm. Results of this analysis are presented in the original guideline document. Finally, an updated MEDLINE search (May 2003 to February 2004) did not identify any studies that have been published since the completion of the formal CCOPGI literature review in May 2003 that would affect the recommendations.

### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

### DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The entire Panel met twice for the purpose of performing an initial review of the materials provided by Cancer Care Ontario (CCO) and to develop a strategy for developing the guidelines. The purpose of the second meeting was to critically evaluate all of the literature to identify the data relevant to the question and to decide on Panel recommendations. All members of the Panel participated in the preparation of the draft guideline document, which was then disseminated for review by the entire Panel.

### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

### METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft guideline document was disseminated for review by the entire Panel. Feedback from external reviewers was also solicited. The content of the guidelines and the manuscript was reviewed and approved by the Health Services Committee (HSC) and by the American Society of Clinical Oncology (ASCO) Board of Directors before dissemination.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following recommendations address three principal questions identified by the guideline developers.

### Should all medically fit patients with curatively resected stage II colon cancer routinely receive adjuvant chemotherapy?

The routine use of adjuvant chemotherapy for medically fit patients with stage II colon cancer is not recommended. Neither the Cancer Care Ontario Practice Guideline Initiative (CCOPGI) systematic review of 37 randomized controlled trials (RCTs) and 11 meta-analyses of adjuvant chemotherapy for colon cancer review, nor the CCOPGI meta-analysis of the 12 American Society of Clinical Oncology (ASCO)-selected RCTs found sufficient supporting evidence for the routine use of adjuvant chemotherapy for these patients. Because clinical trials have not demonstrated a significant improvement in survival, inclusion of a surgery-alone control arm in randomized trials for average-risk stage II patients remains justifiable. At the same time, the oncology research community has recently focused efforts on the conduct of trials to better establish the role of molecular prognostic and predictive factors. The motivation behind these trials is the identification of those patients who are most likely to benefit from treatment by virtue of their high risk of recurrence and/or high probability of response to treatment.

### Should patients with curatively resected stage II colon cancer and with identifiable characteristics that predict for a poor prognosis (i.e., high-risk patients) be offered adjuvant chemotherapy?

Direct evidence from randomized controlled trials does not support the use of adjuvant chemotherapy, even for patients with high-risk stage II colon cancer. Patients and oncologists might reasonably be reluctant to choose adjuvant therapy because of this lack of direct evidence of benefit. However, patients and oncologists who are prepared to take the risk of accepting the results from stage III disease as adequate indirect evidence of benefit are justified in considering the use of adjuvant chemotherapy in stage II disease, provided that they understand that the magnitude of benefit as measured in absolute improvement in survival, is small. Patients who have had a complete resection can be reassured that adjuvant treatment for typical stage II disease does not improve 5-year survival by more than an absolute 5%. Whether smaller incremental improvements in survival can be derived from treatment remains open to question.

In either case, the clinical decision should be based on a discussion with the patient about the nature of the direct evidence supporting treatment, the assumptions inherent in accepting indirect evidence of benefit, the anticipated morbidity of treatment, the presence of high-risk prognostic features, and patient preferences. The optimal approach remains to encourage patients with stage II disease who are facing this decision to participate in randomized trials.

### What strategies can medical and surgical oncologists use to discuss the issue of adjuvant chemotherapy with their patients in clinical practice?

The Panel emphasizes that the treatment decision-making process in stage II colon cancer must incorporate patient choice. The responsibility of the oncologist

is to estimate the risk of recurrence and cancer-related death with and without chemotherapy and to help the patient make an informed decision. Discussion should center on whether the potential benefits of treatment outweigh the potential risks.

Treatment decision making with all stage II patients should include an assessment of other medical problems and anticipated life expectancy. When life expectancy is limited by comorbid illness or very old age, adjuvant treatment offers less potential benefit. To further refine the individual risk for a patient, tools incorporating T and N stage (tumor characteristics) with age and tumor differentiation may also be one way for patients and their physicians to begin discussions about the individual´s risk of recurrence and death. Table 3 in the original guideline document provides a summary of suggested points of discussion between physicians and patients on the value of adjuvant chemotherapy for stage II colon cancer.

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Randomized controlled trials, meta-analyses of randomized controlled trials and Panel consensus

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Familiarity with the evidence regarding the use of adjuvant chemotherapy for stage II colon cancer
- Improved identification of patients with poor prognosis who may benefit
- Increased patient participation in clinical trials
- Improved communication between oncologists and patients regarding the benefits and risks of adjuvant chemotherapy for stage II colon cancer

### POTENTIAL HARMS

For most patients, adjuvant treatment is well tolerated, and the primary hardship is the $\geq$6-month duration of typical adjuvant regimens. Adjuvant therapy typically causes moderate fatigue and gastrointestinal complaints. More severe toxicities of fluorouracil (FU)-based therapy that may require hospitalization, such as mucositis and myelosuppression, are unusual, but, in rare circumstances, they can be life-threatening. The mortality rates associated with adjuvant treatment are in the 1% range and seem to be higher among elderly people.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

The American Society of Clinical Oncology considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician, in light of each patient´s individual circumstances. In addition, these guidelines describe administration of therapies in clinical practice; they cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease for which better therapy is sorely needed. In that guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy

### IOM DOMAIN

Effectiveness
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

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### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Jun 15

## GUIDELINE DEVELOPER(S)

American Society of Clinical Oncology - Medical Specialty Society

## SOURCE(S) OF FUNDING

American Society of Clinical Oncology (ASCO)

## GUIDELINE COMMITTEE

American Society of Clinical Oncology (ASCO) Stage II Adjuvant Chemotherapy Expert Panel

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Al B. Benson III, MD (Co-Chair) Northwestern University Feinberg School of Medicine; Daniel G. Haller, MD (Co-Chair) University of Pennsylvania Cancer Center; Alfred M. Cohen, MD, Lucille P. Markey Cancer Center; Alvaro Tell Figueredo, MD, Hamilton Regional Cancer Centre; Patrick J. Flynn, MD, Minnesota Oncology Hematology P.A.; Monika K. Krzyzanowska, MD ,Dana-Farber Cancer Institute; Jean Maroun, MD, Ottawa Regional Cancer Center; Pamela McAllister, PhD, Marti Nelson Cancer Foundation; Deborah Schrag, MD, Memorial Sloan-Kettering Cancer Center; Eric Van Cutsem, MD, PhD, University Hospital Gasthuisberg, Belgium; Melissa Brouwers, PhD, Ex-Officio, McMaster University; Manya Charette, Ex-Officio, McMaster University

Primary Authors: Al B. Benson III; Deborah Schrag; Mark R. Somerfield; Alfred M. Cohen; Alvaro T. Figueredo; Patrick J. Flynn; Monika K. Krzyzanowska; Jean Maroun; Pamela McAllister; Eric Van Cutsem; Melissa Brouwers; Manya Charette; Daniel G. Haller

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The following authors or their immediate family members have indicated a financial interest. No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. Acted as a consultant within the last 2 years: Patrick J. Flynn, Genentech; Daniel G. Haller, Sanofi-Synthelabo, Pharmacia, Pfizer. Performed contract work within the last 2 years: Al B. Benson III, Sanofi, Pfizer; Daniel G. Haller, Sanofi-Synthelabo, Pharmacia, Pfizer. Received more than $2,000 a year from a company for either of the last 2 years: Al B. Benson III, Sanofi,Pfizer; Patrick J. Flynn, Speakers Bureau, Sanofi, Genentech, Amgen; Jean Maroun, Roche, Pfizer; Daniel G. Haller, Sanofi-Synthelabo, Pharmacia, Pfizer.

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Society of Clinical Oncology (ASCO) Web site.

Print copies: Available from ASCO, Health Services Research, 1900 Duke Street, Suite 200, Alexandria, VA 22314.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Adjuvant therapy for stage II colon cancer: a systematic review from the Cancer Care Ontario Program in Evidence-Based Care´s Gastrointestinal Cancer Disease Site Group. 2004.

Print copies: Available from ASCO, Health Services Research, 1900 Duke Street, Suite 200, Alexandria, VA 22314.

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on August 11, 2004. The information was verified by the guideline developer on August 13, 2004.

## COPYRIGHT STATEMENT



Date Modified: 11/15/2004